

L3 ANSWER 9 OF 9 CANCERLIT on STN
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 AUTHOR: Siddiqui N A; Dunlop W; Thomas E J; Redfern C P
 CORPORATE SOURCE: Dept. of Obstetrics and Gynecology, Univ. of Newcastle upon Tyne, UK.
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AB Over 3500 cases of endometrial carcinoma are diagnosed in the UK per annum. The 5-yr survival rate for all stages of the disease is 70%. Although this seems encouraging, audit reveals that survival rates have not improved in the past 20 yr. This is mainly because current methods of treatment frequently do not deal with lymphatic **metastases**. Improving our understanding of the pathogenesis of this tumor will allow new drugs to be developed and be used as an adjuvant to surgery. Differentiation therapy with retinoids is one such possibility. Retinoic acid, one of the most potent of the naturally occurring retinoids (derivatives of retinol) regulates epithelial cell growth and differentiation. The interest in retinoic acid as an antitumor agent stems from its ability to promote the differentiation of human neuroblastoma and melanoma cells, and to inhibit the growth of breast and lung cancer cells. We have used northern blotting to measure the expression of retinoic acid receptors (RAR), retinoid X receptors (RXR), cellular retinol binding protein type I (CRBP I), and cellular retinoic acid binding proteins I and II (CRABP I and II). 35 samples were collected from patients undergoing hysterectomy. These consisted of 31 endometrioid adenocarcinoma samples of which 12 were grade 1, 10 grade 2 and 9 grade 3 tumors. 4 samples were obtained from patients with severe atypical hyperplasia. Patterns of expression of the receptors have been compared with the expression in histologically normal endometrial stromal and epithelial cells. Patterns of expression in a grade 3 human endometrial adenocarcinoma cell line, **KLE**, have also been studied. mRNA for RAR-alpha, RAR-beta, RAR-gamma, RXR-alpha, RXR-beta, CRBP I, and CRABP II was detected in histologically normal and abnormal endometrium with no differences in expression patterns. Conversely, CRABP I was only detected in 2 grade 2 tumors where myometrial invasion was extensive, and 5 grade 3 tumors and in **KLE** cells, but not in normal endometrium. These results suggest a role for retinoic acid in the etiology of less differentiated tumors.